ISRCTN42305247 https://doi.org/10.1186/ISRCTN42305247

Antidepressant Controlled Trial for Negative Symptoms in schizophrenia

Submission date	Recruitment status
12/05/2010	No longer recruiting
Registration date	**Overall study status**
12/05/2010	Completed
Last Edited	**Condition category**
03/06/2016	Mental and Behavioural Disorders

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Schizophrenia is a mental health problem usually starting in the late teens or early twenties, and often lasting many years. It affects behaviour, thinking and perception, and in more severe cases it affects a person's ability to socialise, work and carry out routine daily tasks appropriately. The best known features of schizophrenia are 'positive' symptoms such as false beliefs ('delusions') and hallucinations (most commonly, hearing voices). But also common are the so-called 'negative' symptoms, which appear to reflect a loss of a person's usual emotional expressiveness and responsiveness, spontaneity of speech, and drive. These can affect a person's ability to relate to other people and get on with day-to-day tasks. The standard medication ('antipsychotics') is usually helpful for this illness, and if taken continually over time can keep people well, reducing the likelihood of further episodes. However, the positive symptoms tend to be more likely to improve with this medication than the negative symptoms, and so a proportion of people with schizophrenia, perhaps around 1 in 5, will have continuing negative symptoms. If antipsychotic medication alone does not help negative symptoms for a particular person, there are no other established medications that we know can help. However, there is some evidence that antidepressant medication, usually given to treat depression, might also reduce negative symptoms if added to antipsychotic medication, and not produce too many problems with side effects. What is not clear is whether any improvement in negative symptoms is also accompanied by an improvement in a person's quality of life, and how long it might take for that to be evident. The evidence mainly comes from research studies where an antidepressant was added to antipsychotic medication over a relatively short period, and no longer than three months. These studies have reported any changes observed in negative symptoms but not whether there was any effect on a person's quality of life. Also, not all of these studies have carefully distinguished whether any improvement seen is specific to negative symptoms or due to change in other symptoms of schizophrenia or side effects of antipsychotic medication, which can all look very similar. We plan to carry out a study which will try to overcome these limitations of previous studies.

Who can participate?
Patients aged 18 – 75 with schizophrenia who are being treated with antipsychotic medication but are experiencing continuing negative symptoms

What does the study involve?
Participants are randomly allocated to have either an antidepressant (citalopram) or a dummy tablet (placebo) added to the antipsychotic medication that they are already receiving, for a year. We have chosen citalopram as the antidepressant because while there is no reason to think that one antidepressant is likely to work better than another, citalopram is one of the least likely to cause problems by interacting with antipsychotic medication. By carefully assessing all the relevant symptoms and side effects regularly over the year of treatment and comparing those people taking the antidepressant with those given the placebo, we should be able to see if the antidepressant has had any effect on quality of life or negative symptoms. Also, we should gain a greater understanding of any positive effects of adding an antidepressant to antipsychotic treatment on a person's ability to live and work in the community, as well as the possible risks with regard to side effects.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
June 2010 to December 2011

Who is funding the study?
Health Technology Assessment Programme (UK)

Who is the main contact?
Prof. Thomas Barnes

Contact information

Type(s)
Scientific

Contact name
Prof Thomas Barnes

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Additional identifiers

Clinical Trials Information System (CTIS)
2009-009235-30

ClinicalTrials.gov (NCT)

NCT01032083

Protocol serial number
HTA 07/83/01; 7155

Study information

Scientific Title
A multicentre randomised interventional trial of the clinical and cost-effectiveness of citalopram versus placebo in the management of negative symptoms of schizophrenia

Acronym
ACTIONS

Study objectives
The ACTIONS study is a multi-centre, double-blind, placebo-controlled, randomised clinical trial. The main aim of the study is to establish the clinical and cost-effectiveness of the selective serotonin reuptake inhibitor (SSRI) antidepressant, citalopram, in the management of negative symptoms of schizophrenia. The research hypothesis to be tested is that augmentation of stable antipsychotic medication with citalopram, is clinically and cost-effective for ameliorating persistent negative symptoms in schizophrenia and is not associated with an additional side effect burden.

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/078301
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0018/51930/PRO-07-83-01.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
Charing Cross Research Ethics Committee, 21/08/2009, ref: 09/H0711/81

Study design
Multicentre randomised interventional treatment trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Mental Health Research Network; Subtopic: Schizophrenia; Disease: Schizophrenia

Interventions
Participants will be randomly assigned to receive additional treatment with either citalopram or identical placebo. Treatment with citalopram will be initiated at 20 mg/day for the first 4 weeks (or one placebo capsule), followed by the option to increase the dose to 40 mg per day (or two placebo capsules) for the remainder of the study period, i.e. daily for up to a year. If there are

problems with tolerability, the clinician can reduce the dose back to 20 mg/day (or one placebo capsule).

Follow-up length: 12 months
Study entry: single randomisation only

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Citalopram

Primary outcome(s)
PANSS, measured at 3 months and 12 months

Key secondary outcome(s))
1. Mental state
2. Social function
3. Service engagement
4. Medication

All outcomes scales relevant to the secondary outcomes will be administered at baseline and subsequently at 3, 9 and 12 months.

Completion date
01/12/2011

Eligibility

Key inclusion criteria
1. An Operational Criteria Checklist for Psychosis (OPCRIT) diagnosis of schizophrenia, schizophreniform, schizoaffective disorder or psychosis not otherwise specified (NOS) as defined by Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)
2. A negative subscale score of 20 or more on the Positive and Negative Syndrome Scale for Schizophrenia (PANSS). At least three of the seven items on the negative symptom subscale should be rated 3 or more. Negative symptoms that reflect, sometimes very subtly, manifestations of depressive symptoms, antipsychotic side effects such as bradykinesia, or positive symptoms, are referred to as secondary negative symptoms, and the assessors will attempt to distinguish these from primary negative symptoms. However, persistent negative symptoms will be used as an inclusion criterion rather than primary negative symptoms, as the former are the clinically-relevant target, and the latter represent a hypothesis about aetiology that cannot be definitely determined on cross-sectional assessment.
3. Aged 18 - 75 years, inclusive, either sex
4. Clinically stable for the last 3 months with a consistent antipsychotic regimen
5. Competent and willing to provide written, informed consent

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Any medical contraindications to an SSRI antidepressant
2. Currently receiving antidepressant or clinician wants to treat with an antidepressant
3. Currently fulfil criteria for major depressive disorder; alcohol/substance hazardous use or dependence in past 3 months
4. Treated with ECT in the last 8 weeks
5. Cognitive or language difficulties that would preclude subjects providing informed consent or compromise participation in study procedures

Date of first enrolment
01/06/2010

Date of final enrolment
01/12/2011

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Imperial College London
London
United Kingdom
W6 8RP

Sponsor information

Organisation

Imperial College London (UK)

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/04/2016		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes